REMARKS

Rejections under 35 U.S.C.§112, first paragraph

On page 2, of the Final Office Action, the Examiner maintains the rejection claims 6 and 8-10 under 35 U.S.C.§112, first paragraph for lack of enablement, "for the reasons of record." Applicants traverse this rejection and withdrawal thereof is respectfully requested.

In the response of September 8, 1999, Applicants presented specific arguments addressing this rejection. However in the final Office Action, the Examiner fails to in any way address or rebut Applicants arguments. It is insufficient to simply state that the rejection is maintained for the reasons of record without responding to the arguments presented and supporting why the arguments are insufficient to overcome the rejection. Applicants arguments were fully responsive to this rejection, as such the Examiner is requested to please specifically address and rebut the presented arguments or withdraw the rejection.

Rejections under 35 U.S.C.§112, second paragraph

The Examiner additionally maintains the rejection of claims 8-10 under 35 U.S.C. §112, second paragraph. However, as with the rejections under 35 U.S.C. §112, first paragraph, the Examiner fails to provide any rebuttal of Applicants' two and a half pages of remarks,

which addressed each point raised by the Examiner for the rejection of claims 8-10. In addition, Applicants note that claims 8-10 were rejected for more than one issue under 35 U.S.C.§112, second paragraph and it is not clear to Applicants if all rejections are being maintained or only some. Applicants respectfully request that the rejection be withdrawn or that the Examiner rebut the remarks of September 8, 1999 and specifically point out the inadequacy of the remarks so that Applicants may have some guidance in how to proceed.

Claims 8 and 9 have been rejected for lacking antecedent basis for "crosslinkable oligonucleotides." Claims 8 and 9 have been to recite "conjugatable" for consistency with the other claims and to provide proper antecedent basis for all terms. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§102(e) and 103

The Examiner maintains the rejection of claims 1 and 3-5 under 35 U.S.C. §§102 or 103 (as indicated) over either Birkenmeyer et al., Nickerson et al., Delahunty et al., Kwok et al. and Nilsson et al.

With regard to Birkenmeyer et al., the Examiner appears to be interpreting the amplification of the DNA as inherently meeting the

present feature of only obtaining a signal when the second and third affinity reagents are closely bound on the same macromolecule.

With regard to Kwok et al., Nickerson et al. and Nilsson et al., the Examiner asserts that these references teach probes which will only generate a signal if two affinity reagents are bound sufficiently close to each other.

Applicants traverse these rejections and withdrawal thereof is respectfully requested. As indicated in the Abstracts of each of the cited references, Birkenmeyer et al., Nickerson et al., Delahunty et al., Kwok et al. and Nilsson et al. all pertain to the detection of nucleic acid sequences, i.e. with all of these references nucleic acid sequences are the target molecules, not the probes. The nucleic acids in all of these references are the "specific macromolecule" of claim 1 and the "specific antigen" of claim 6. In these references, it is the target molecule which is being amplified, not the probe molecule. There is no suggestion in these references of using two probe molecules (affinity reagents) which will generate a signal by nucleic acid amplification only if the second and third probe molecules are closely bound to the target macromolecule. As such, there is no disclosure or suggestion in Birkenmeyer et al., Nickerson et al., Delahunty et al., Kwok et al. or Nilsson et al. of the

present invention and the present invention is therefore not obvious over these references.

The Examiner further maintains the rejection of claims 1-6 and 8 and 1-4 under 35 U.S.C. §103 as being obvious over Lee et al. in view of Dattagupta and Ciechanover et al. Applicants acknowledge that Lee et al. discloses the use of multiple antibodies to different epitopes on an antigen. However, as clearly shown in Figures 5 and 6 of Lee et al. there is no need for the antibodies to the bind in close proximity on the target antigen to create a signal. In fact, as shown in Figures 5 and 6 the antibodies can bind on fully opposite sites of the target antigen. With Lee et al. none of the affinity reagents are actually interacting with each other directly to produce a signal. Thus, Lee et al. fail to teach signal production only when the second and third affinity reagents (antibodies) are closely bound on the same macromolecule. Dattagupta et al. and Ciechanover et al. pertain to the use of nucleic acid probes and amplification of a signal by using nucleic acid probes. However, neither Dattagupta et al. nor Ciechanover et al. teach that amplification (signal) only occurs if two separate affinity reagents are closely bound on the same target macromolecule. As such, Dattagupta et al. and Ciechanover et al. fail to overcome the deficiencies of Lee et al. and the present invention is

not achieved by combining the references. Withdrawal of the rejection is therefore respectfully requested.

Finally, claims 1-4 remain rejected under 35 U.S.C.§103 as being obvious over Hendrickson et al. Hendrickson et al. discloses a "multianalyte immunoassay" for detecting three different analytes. See Abstract. The immunoassay of Hendrickson et al. uses nucleic acid conjugated antibodies as probes. However, Hendrickson et al. fails to teach the feature of the present invention that amplification of the nucleic acid probes only takes place and thus signal is only generated if two different antibodies are sufficiently closely bound to the same target antigen.

By requiring the binding of two different affinity reagents in sufficiently close proximity to one another before signal will be generated, the present invention renders most non-specifically bound affinity reagents incapable of generating a signal because most non-specific binding will be at a distance too great to initiate amplification. There is no disclosure or suggestion in Hendrickson et al. of this feature of the present invention or the advantages associated therewith. As such, the present invention is not obvious over Hendrickson et al.

As the above-presented amendments and remarks address and overcome the rejections of the Examiner, withdrawal of the rejections and

reconsideration and allowance of the claims are respectfully requested. Should the Examiner have any questions regarding the present application, she is requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) in the Washington DC area, at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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